

Amendments to the Specification:

Please **replace** Table 1, page 19 with the following Table 1

SEQ ID NO:	Name	Description	Sequence
1	SEQ ID NO:1	PAX2 15 mer fragment-D form retroinversion	rtlrrnhsshkant
2	SEQ ID NO:2	P31 16 mer fragment- D form retroinversion	gphrrgrpnsrskrt
3	SEQ ID NO:3	HAX42 14 mer fragment- D form retroinversion	gtsngngccnydgp
4	SEQ ID NO:4	PAX2 15 mer fragment	TNAKHSSHNRRLRTR
5	SEQ ID NO:5	P31 16 mer fragment	TRKSSRSNPRGRRHPG
6	SEQ ID NO:6	HAX42 14 mer fragment	PGDYNCCGNGNSTG
9	ZElan144	dansylated PAX2 15 mer fragment-D form retroinversion	K(dns)-rtlrrnhsshkant
10	ZElan145	dansylated P31 16 mer fragment- D form retroinversion	K(dns)-gphrrgrpnsrskrt
11	ZElan146	dansylated HAX42 14 mer fragment- D form retroinversion	K(dns)-gtsngngccnydgp
12	ZElan129	dansylated PAX2 15 mer fragment	K(dns)- TNAKHSSHNRRLRTR
13	ZElan031	dansylated P31 16 mer fragment	K(dns)- TRKSSRSNPRGRRHPG
14	ZElan091	dansylated HAX42 14 mer fragment	K(dns)- PGDYNCCGNGNSTG

Please **replace** Table 3, page 21 with the following Table 3:

Name	Sequence	K _D (μmol)
ZElan018	K(dns)-STPPSREAYSRPYSVDSDDTNAKHSSHNRRLRTRSRPNG (SEQ ID NO:7)	>50.0
ZElan129	K(dns)-TNAKHSSHNRRLRTR (SEQ ID NO:12)	29.6
ZElan144	K(dns)-rtrlrnhsshkant (SEQ ID NO:9)	28.8
ZElan021	K(dns)-SDHALGTNLRSDNAKEPGDYNCCGNGNSTGRKVFNRRRPSAIP (SEQ ID NO:8)	6.7
ZElan091	K(dns)-PGDYNCCGNGNSTG (SEQ ID NO:14)	0.75
ZElan146	K(dns)-gtsngngccnydgp (SEQ ID NO:11)	21.65

Please **replace** the paragraph at page 20, line 22 to page 21, line 2, already amended on October 5, 2001, with the following paragraph:

04
-- ZElan021, full length HAX42 [K(dns)-SDHALGTNLRSDNAKEPGDYNCCGNGNSTGRKVFNRRRPSAIP] (SEQ ID NO:53; dansylated version is SEQ ID NO:8) was given the arbitrary value of 1.00 for binding to P100 at a given peptide concentration determined from the signal-to-noise ratio data. Table 2 shows the results of P100 assays with the HAX42 related peptides ZElan021, ZElan091 and ZElan146. Assay number 1 was at 20 µg/ml; 2 and 3 were at 50 µg/ml; and 4 through 8 were at 25 µg/ml. The results for the retro-inverted form, ZElan 146 show reasonable binding compared to the HAX42 fragment ZElan091 and that the activity of the GIT targeting agent was not eliminated when converted to its retro-inverted form. --

Please **replace** the paragraph at page 21, lines 5-11, already amended on October 5, 2001, with the following paragraph:

05
--K_D values, or the concentration of the peptide required to reach half maximal binding to Caco-2 P100 fractions, are given in Table 3 for ZElan021, full length HAX42, [K(dns)-SDHALGTNLRSDNAKEPGDYNCCGNGNSTGRKVFNRRRPSAIP] (SEQ ID NO:53; dansylated version is SEQ ID NO:8), HAX42 fragment ZElan091, and the retro-inverted form of this fragment, ZElan146 as well as for ZElan018, full length PAX2, [K(dns)-STPPSREAYSRPYSVDS DSDTNAKHSSHNRRLRTRSRPNG] (SEQ ID NO:7; dansylated version is SEQ ID NO:15), PAX2 fragment ZElan129, and the retro-inverted form of this fragment, ZElan144.--

On page 5, after line 12, please **insert** the following paragraphs:

-- The HPT1, hPEPT1, D2H, and hSI receptors were selected for cloning as GIT receptor targets based on several criteria, including: (1) expression on surface of epithelial cells in gastro-intestinal tract (GIT); (2) expression along the length of small intestine (HPT1, hPEPT1, D2H); (3) expression locally at high concentration (hSI); (4) large putative extracellular domains facing into the lumen of the GIT; and (5) extracellular domains that permit easy access and bioadhesion by targeting particles.

The four recombinant receptor sites screened with the peptide libraries additionally have the following characteristics:

<u>Receptor</u>	<u>Characteristics</u>
D2H	Transport of neutral/basic amino acids; a transport activating protein for a range of amino acid translocases
hS1	Metabolism of sucrose and other sugars, represents 9% of brush border membrane protein Jejunum
HPT1	di/tri peptide transporter or facilitator of peptide transport
hPEPT1	di/tri peptide transporter

6.2. Cloning of Extracellular Domain of Selected Receptor Site

The following receptor domains were cloned and expressed as His-tag fusion proteins by standard techniques:

<u>Receptor</u>	<u>Domain (amino acid residues)</u>
hPEPT1 ^a	391-571
HPT1 ^b	29-273
hSI ^c	272-667
D2H ^d	387-685

^a Liang et al., 1995, J. Biol. Chem. 270: 6456-6463;

^b Dantzig et al., 1994, Association of Intestinal Peptide Transport with a Protein Related to the Cadherin Superfamily;

- ^c Chantret et al., Biochem. J. 285: 915-923;
^d Bertran et al., J. Biol. Chem. 268: 14842-14949.

The receptor proteins were expressed as His-tag fusion proteins and affinity purified under denaturing conditions, using urea or guanidine HCl, utilizing the pET His-tag metal chelate affinity for Ni-NTA Agarose (Hochuli, E., Purification of recombinant proteins with metal chelate adsorbent, Genetic Engineering, Principals and Methods (J.K. Setlow, ed.), Plenum Press, NY, Vol. 12 (1990), pp. 87-98).

As indicated in WO 98/51325, phage which showed specificity to a GIT receptor was further characterized by ELISA on a variety of recombinant proteins. Phage which continued to exhibit GIT receptor specificity was sequenced. Their insert sequences are summarized as follows:

	SEQ.	
<u>hSI</u>	<u>ID.NO</u>	<u>TARGET BINDING PHAGE INSERT SEQUENCE</u>
S15	16.	RSGAYESPDGRGGRSYVGGGGGCGNIGRKHNLWGLRTASPACWD
S21	17.	SPRSFWPVVSRHESFGISNYLGCGYRTCISGTMTKSSPIYPRHS
S22	18.	SSSSDWGGVPGKVVRERFKGRGCGISITSVLTGKPNPCPEPKAA
Sni10	19.	RVGQCTDSDVRRPWARSCAHQGCGAGTRNSHGCITRPLRQASAH
Sni28	20.	SHSGGMNRAYGDVFRELDRWNATSHHTRPTPQLPRGPN
Sni34	21.	SPCGGSWGRFMQGGFLGGRTDGCGAHRNRTSASLEPPSSDY
Sni38	22.	RGAADQRRGWSENLGLPRVGWDAIAHNSYTFTSRRPRPP
Sni45	23.	SGGEVSSWGRVNDLCARVSWTGCGTARSARTDNKGFLPKHSSLR
SniAX2	24.	SDSDGDHYGLRGGVRCSLRDRGCGLALSTVHAGPPSFYPKLSSP
SniAX4	25.	RSLGNYGVTGTVDVTVLPMPGHANHLGVSSASSSDPPRR
SniAX6	26.	RTTTAKGCLLGSFGVLSGCSFTPTSPPPHLGYPPHSVN
SniAX8	27.	SPKLSSVGVMTKVTELPTEGPNAISIPI SATLGPRNPLR

D2H

DAB3 28. RWCGAELCNSVTKKFRPGWRDHANPSTHHRTPPPSQSSP
DAB7 29. RWCGADDPGASRWGGSNSLFGCGLRCSAAQSTPSGRIHSTSTS
DAB10 30. SKSGEGGDSSRGETGWARVRSHAMTAGRFRWYNQLPSDR
DAB18 31. RSSANNCEWKSDWMRRACIARYANSSGPARAVDTKAAP
DAB24 32. SKWSWSSRWGSPQDKVEKTRAGCGGSPSSTNCHPYTFAPPPQAG
DAB30 33. SGFWEFSRGLWDGENRKSVRSGCGFRGSSAQGPCVTPATIDKH
DAX15 34. SESGRCSRVSRWMTTWQTQKGGCGSNVSRGSPLDPSHQTGHATT
DAX23 35. REWRFAGPPLDLWAGPSLPSFNASSHPRALRTYWSQRPR
DAX24 36. RMEDIKN SGWRDSCRWGDLRPGCGSRQWYPSNMRSSRDYPAGGH
DAX27 37. SHPWYRHWNHGDFSGSGQSRHTPPESPHPGRPNATI
DCX8 38. RYKHDIGCDAGVDKKSSSVRGGCGAHSSPPRAGRGRGTMTVSRL
DCX11 39. SQGSKQCMQYRTGRLTVGSEYGCGMNPARGHATPAYPARLLPRYR
DCX26 40. SGRTTSEISGLWGWGDDRS GYGWGNLRLPNYIPYRQATNRHRYT
DCX33 41. RWNWTVLPATGGHYWTRSTDYHAINNHRPSIPHQHPTPI
DCX36 42. SWSSWNWSSKTTRLGDRATREGCGPSQSDGCPYNGRLTTVKPRT
DCX39 43. SGSLNAWQPRSWVGGAFRSHANNLNPKPTMVTRHPT
DCX42 44. RYSGLSPRDNGPACSQEATLEGCGAQRLMSTRRKGRNSRPGWTL
DCX45 45. SVGNDKTSRPVSFYGRVSDLWNASLMPKRTPPSSKRHDDG

hPEPT1

PAX9 46. RWPSVGKYGNGSDTIDVHSNDASTKRSLIYNHRRPLFP
PAX14 47. RTFENDGLGVGRSIQKKSDRWYASHNIRSHFASMSPAGK
PAX15 48. SYCRVKGGGEGGHTDSNLARSGCGKVARTSRLQHINPRATPPSR
PAX16 49. SWTRWKGKTHGGFVNKSPPGKNATSPYTDAQLPSDQGPP

PAX17 50. SQVDSFRNSFRWYEPSRALCHGCGKRDSTTRIHNSPSDSYPTR
 PAX18 51. SFLRFQSPRFEDYSRTISRLRNATNPSNVSDAHNNRALA
 PAX35 52. RSITDGGINEVDLSSVSNVLENANSHRAYRKHRPTLKRP
 PAX38 53. SSKVSSPRDPTVPRKGGNVDYGCGRSSARMPTSALSSITKCYT
 PAX40 54. RASTQGGRGVAPEFGASVLGRGCGSATYYTNSTSCKDAMGHNYS
 PAX43 55. RWCEKHKFTAARCSAGAGFERDASRPPQPAHRDNTNRNA
 PAX45 56. SFQVYPDHGLERHALDGTGPLYAMPGRWIRARPQNRDRQ
 PAX46 57. SRCTDNEQCPDTGTRSRSVSNARYFSSRLLKTHAPHRP
 P31 58. SARDSGPAEDGSRAVRLNGVENANTRKSSRSNPRGRRHP
 P90 59. SSADAEKCAGSLLWWGRQNNSGCGSPTKKHLKHRNRSQTSSSSH
 5PAX3 60. RPKNVADAYSSQDGAAAEETSHASNAARKSPKHKPLRRP
 5PAX5 61. RGSTGTAGGERSGVLNLHTRDNASGSGFKPWYPSNRGHK
 5PAX7 62. RWGWERSPSDYDSDMDLGARRYATRTHRAPPVRLKAPLP
 5PAX12 63. RGWKCEGSQAAYGDKDIGRSRGCGSITKNNTNHAHP SHGAVAKI

HPT-1

HAX9 64. SREEANWDGYKREMSHRSRFWDATHLSRPRRPANSGDPN
 HAX35 65. EWYSWKRSSKSTGLGDTATREGCGPSQSDGCPYNGRLTTVKPRK
 HAX40 66. REFAERRLWGCDDLSWRLDAEGCGPTPSNRAVKHRKPRPRSPAL
 HAX42 67. SDHALGTNLRSDNAKEPGDYNCCGNGNSTGRKVFNRRRPSAIP
 HCA3 68. RHISEYSFANSHLMGGESKRKGCGINGSFSPTCPRSPTPAFRRT
 H40 69. SRESGMWGSWWRGHRLNSTGGNANMNASLPPDPPVSTP
 PAX2 70. STPPSREAYSRPYSVDSDSDTNAKHSSHNRRLRTRSRPN

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On page 6, after line 14, please **insert** the following paragraph:

① --In a specific embodiment of the invention, proteins consisting of or, alternatively, comprising all or a fragment of a GIT transport receptor-binding peptide consisting of at least 5, 10, 15, 20, 25, 30 or 35 (contiguous) amino acids of the full-length GIT transport receptor-binding peptide are provided. In a specific embodiment, such proteins are not more than 20, 30, 40, 50, or 75 amino acids in length. Derivatives or analogs of GIT transport receptor-binding peptides include but are not limited to those molecules comprising regions that are substantially homologous to GIT transport receptor-binding peptides or fragments thereof (e.g., at least 50%, 60%, 70%, 80% or 90% identity) (e.g., over an identical size sequence or when compared to an aligned sequence in which the alignment is done by a computer homology program known in the art) or whose encoding nucleic acid is capable of hybridizing to a coding GIT transport receptor-binding peptide sequence, under stringent, moderately stringent, or nonstringent conditions. --

To see how changes were made in Tables 1 and 3 and replaced paragraphs, please go to Amendments with Markings Showing Changes on Page 32.